

Magnetic Resonance Imaging Based Evaluation of Diagnostic Accuracy of Dual-energy Computed Tomography for Intracranial High Density Areas After Mechanical Thrombectomy

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After mechanical thrombectomy (MT) for acute ischemic stroke, contrast extravasation may be observed. Therefore, the diagnosis of intracranial hemorrhage (ICH) as the complication is difficult via conventional computed tomography (CT). This study aimed to evaluate the diagnostic accuracy of dual-energy CT (DECT) in differentiating ICH from contrast extravasation after MT. A retrospective study was conducted on patients who underwent MT from January 2019 to May 2022. Single-energy CT and DECT were conducted to estimate the ICH immediately after MT. Diagnostic confirmation of ICH and the diagnostic accuracy of DECT were evaluated via magnetic resonance imaging (MRI). Fifty-eight patients were assigned to this study. One patient (1.7%) had symptomatic ICH, and 18 (31.0%) had asymptomatic. The diagnostic accuracy of DECT based on MRI was 52.6% for sensitivity and 97.4% for specificity. Although DECT has been indicated to have high specificity for diagnosing

hemorrhage after MT, MRI-based studies of DECT need improvement.

Keywords: intracranial hemorrhage, dual-energy computed tomography, magnetic resonance imaging, mechanical thrombectomy, acute ischemic stroke

INTRODUCTION

Mechanical thrombectomy (MT), as the application of neuroendovascular therapy, is an effective treatment for acute cerebral infarction caused by large cerebral vessel occlusion [1–3]. However, hemorrhagic complications such as subarachnoid and intraparenchymal hemorrhage can occur at a certain rate. These conditions can occur due to cerebral vessel perforation caused by microguide wire and retraction injury of cerebral perforating arterioles caused by traction force during clot retrieval [1, 4]. On the other hand, MT needs frequent cerebral angiography with injection of contrast medium and extravascular leakage of the medium can occur due to the disruption of the local blood–brain barrier caused by acute cerebral ischemia. Since both hemorrhagic complications and extravasation of the contrast material are usually depicted as similar high density lesions in the subarachnoid spaces or brain parenchyma, it

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is difficult to distinguish hemorrhagic complication from contrast agent extravascular leakage via conventional single-energy CT (SECT) scans [5].

Recently, dual-energy CT (DECT) has been emerged. This novel CT scan system uses two different X-ray energies to the target part of the body and can obtain different X-ray absorption values from the same object [6]. It can generate clinically significant imaging data that could not possible with SECT, and its high discriminative ability with respect to the object being imaged makes it useful for differentiating blood, contrast media, and calcification [7]. Nowadays, some reports stated that DECT is useful to distinguish the hemorrhagic complication from contrast leakage after endovascular treatment, especially MT [8, 9]. It is well known that MRI has highest diagnostic power for cerebral hemorrhage [10]. MRI imaging should be taken in immediate after MT to detect cerebral hemorrhage precisely, however, evaluation with MRI is not rarely possible because of unstable vital signs and restlessness of the patients after MT. Therefore, DECT tend to conduct as an alternative examination, but there are not many studies on its diagnostic accuracy. Previous studies have evaluated the diagnostic accuracy of DECT using follow-up SECT as reference images. At the moment, there are very few data comparing DECT findings with MRI. The purpose of our study was to validate the diagnostic accuracy of DECT for hemorrhagic complications and contrast extravasation after MT based on MRI findings.

MATERIALS AND METHODS

Patient Population

We retrospectively analyzed patients with acute cerebral infarction caused by large cerebral vessel occlusion and treated with MT at National Hospital Organization Hamada Medical Center between January 2019 and May 2022. Patients in this study who received both SECT and DECT immediately after MT, and further were underwent follow-up MRI within 24 h. The exclusion criteria of this study were the patients who could not undergo DECT at the discretion of the surgeon or could not take MRI for metallic implant or pacemaker implantation.

Treatment

Indication for mechanical thrombectomy was based on the Japanese Guideline for the Management of Stroke 2021 [11]. The operator who conducted the MT was a Japanese society for neuroendovascular therapy board certificated neurointerventionist. Patient's neurological findings were assessed by the National Institutes of Health Stroke Scale score on arrival and the day after the operation. Preoperative diagnosis was performed using SECT and MRI. The ischemic lesions, especially in the anterior circulation, were scored using diffusion weighted imaging-Alberta Stroke Program Early CT Score (DWI-ASPECTS) as a reference for treatment indication [12, 13]. When the basilar or vertebral artery was occluded, the score was evaluated using DWI based on pc-ASPECTS [14].

A bolus of 3,000 units of heparin was injected at the beginning of the intervention with or without intravenous recombinant tissue plasminogen activator (IV rtPA), and the intraoperative ACT was adjusted to a target of 200–250 s. The intervention was performed under local anesthesia via the transfemoral approach. Basically, we used the balloon guiding catheter which was placed at the proximal of the occlusion artery to protect the distal embolism. A stent retriever (e.g., Trevo, Stryker Neurovascular, Raynham, Massachusetts, USA; Solitaire, Medtronic Neurovascular, Irvine, California, USA) or an aspiration catheter (e.g., React, Medtronic Neurovascular, Irvine, California, USA; Catalyst, Stryker Neurovascular, Raynham, Massachusetts, USA) was used as the thrombus retrieval device, and both were used as combined technique at the discretion of the surgeon. Percutaneous transluminal angioplasty (PTA) was performed if the occlusion was due to atherosclerotic stenosis. The results of revascularization were evaluated using the score of Thrombolysis in Cerebral Infarction (TICI), and good recanalization was defined as TICI 2b or 3 [15]. The time from onset to recanalization and the time from puncture for sheath inserting to recanalization were recorded. If the onset time was uncertain, the last time the patient was healthy was used as the reference time. In case of a poor recanalization outcome, such as TICI 0 to 2a, the time of the last clot retrieval procedure was defined as the recanalization time.

Imaging Protocols

SECT and DECT examination were performed just after the procedures on a DECT system (Aquilion One GENESIS Edition, Canon Medical Systems, Tochigi, Japan). The DECT scan parameters were as follows: scanning technique, Dual spin; scan direction, caudocranial; tube voltage, 80 / 135 kVp; current, SD3.5; collimation, 320 × 0.5 mm; rotation time, 1.0 s; pitch, 1.0; dose modulation (volume EC, Canon Medical Systems, Tochigi, Japan). The SECT was performed using a single-energy technique (120 kVp). Reconstruction parameters were as follows: slice thickness, 5.0 mm; reconstruction kernel, FC13; display field of view, 24.0 cm. From these parameters, SECT images, iodine maps and virtual non-contrast (VNC) images were generated.

MRI was performed with a clinically dedicated system at 3.0 T (MAGNETOM Skyra, Siemens AG Medical Group, Erlangen, Germany) using a circular polarized head coil. Intracranial hemorrhage (ICH) was diagnosed based on T2*-weighted gradient-echo sequence (T2*GRE) which of parameters were TR = 700 ms, TE 10 ms, thickness 5.0 mm. Hemorrhagic lesions were defined as low-intensity lesions indicating hemosiderin deposition in the images obtained by T2*GRE.

Imaging Analysis

Postoperative all SECT and DECT images and MRI were evaluated by an experienced radiologist blinded to the clinical data. High density on SECT was defined as areas with objective higher density than the surrounding gray or white matter. DECT imaging findings were classified into two groups as follows. A) DECT-positive: high density on SECT and high density at same location on VNC. This suspects hemorrhagic lesions. B) DECT-negative: High density on SECT and no findings at same location on VNC. This suggests contrast material leakage.

Diagnosis of hemorrhagic complications was confirmed by T2*GRE after the MT within 24 h. All DECT image were referred to T2*GRE and finally evaluated for the hemorrhagic lesion or the contrast medium extravascular leakage. ICH was classified with Heidelberg bleeding classification [16]. Class is simply determined from the width of hemorrhagic transformation in or beyond ischemic brain

parenchyma, and the location of extra-parenchymal bleeding. And in this classification, symptomatic ICH is defined as an increase in the total NIHSS score by 4 or more points or an increase in one of the NIHSS categories by 2 or more points due to new bleeding. Symptomatic ICH in this study was defined in the same way.

Data Collection

The following clinical and radiological data for each patient were extracted from our institutional database. Age, sex, NIHSS on admission, DWI-ASPECTS on admission, IV rtPA administration, site of occluded vessel, type of device used for revascularization, number of revascularization attempts: number of lesions passes, TICI at end of surgery, puncture to recanalization time, onset to recanalization time, distribution of bleeding sites.

Statistical Analysis

All patients who underwent DECT and follow-up MRI were included in the analysis. Patients were divided into positive and negative DECT groups, and hemorrhage and no hemorrhage groups, and the predictive values were calculated. A statistical analyses was performed with EZR, which is for R. More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics [17].

RESULTS

Patients Included in this Study

MT was performed in 73 patients during the study period. Ten patients were excluded because DECT was not received immediately after the treatment and three patients were excluded because MRI could not be done due to their pacemaker implantation. Besides, two patients were excluded because they were judged to be underdiagnosed due to artifacts in the MRI images, finally resulting in 58 patients being included in the study (Fig. 1).

Patients Characteristics

Details of the patients included in this study are shown in Table 1. The mean age of the patients was 77.1 ± 13.2 years, and 22 (43%) were male.

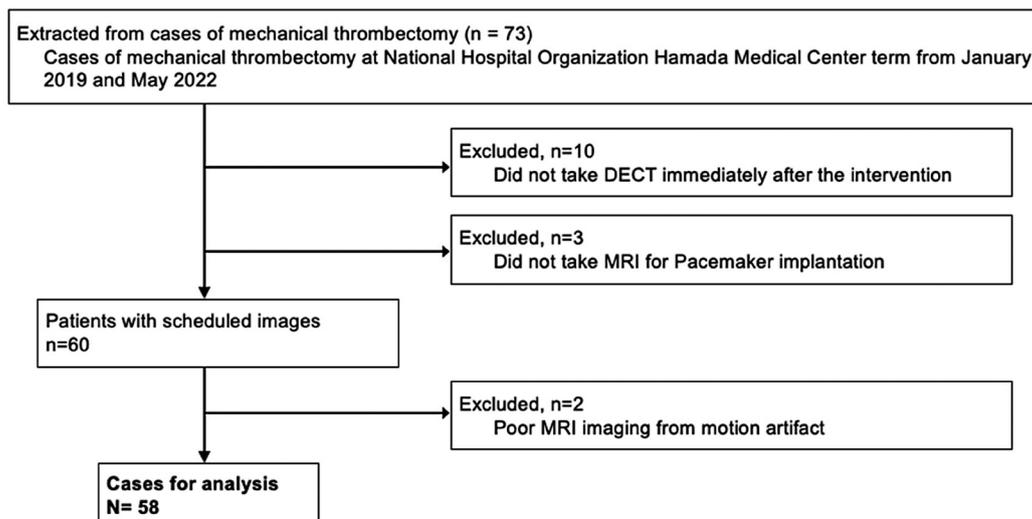


Figure 1. Flowchart of the Study Population

Patients who did not undergo dual-energy CT (DECT) and magnetic resonance imaging (MRI) or could not avail the data were excluded in this study.

Table 1. Patient characteristics

Variable	Overall n = 58
Age (mean), y	77.1 ± 13.2
Male sex (%)	22 (43)
NIHSS on admission	21.2 ± 8.8
DWI-ASPECTS on admission †	7.0 ± 2.2
IV rtPA (n (%))	27 (47)
Occlusion site (n (%))	
Anterior cerebral artery	1 (1.7)
Middle cerebral artery	42 (72.4)
M1	35 (60.3)
M2	7 (12.1)
Internal carotid artery	11 (19.0)
Basilar artery	4 (6.9)
Device for revascularization (n (%))	
Stent retriever	7 (12.1)
Aspiration catheter	4 (6.9)
Combined stent and aspiration devices	47 (81.0)
PTA balloon	5 (8.6)
Passes	1.8 ± 1.1
TICI 2b or 3 (n (%))	53 (91)
Onset to recanalization (min)	323 ± 206
Puncture to recanalization (min)	68.5 ± 33.4
Distribution of hemorrhages based on T2*GRE according to the Heidelberg hemorrhage classification (n (%))	
1a: Scattered small petechiae in infarcted brain tissue	2 (3.4)
1b: Confluent petechiae in infarcted brain tissue	9 (15.5)
1c: Hematoma within infarcted tissue, occupying < 30%	3 (5.2)
2: Intracerebral hemorrhage within and beyond infarcted brain tissue	1 (1.7)
3c: Subarachnoid hemorrhage	4 (6.9)

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; DWI, diffusion weighted imaging; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; IV rtPA, intravenous recombinant tissue plasminogen activator; PTA; percutaneous transluminal angioplasty; TICI, thrombolysis in cerebral infarction; T2*GRE, T2*-weighted gradient-echo MR image

† Exclude posterior circulation score (Pc-ASPECTS)

The mean NIHSS was 21.2 ± 8.8 and DWI-ASPECTS was 7.0 ± 2.2 . However, patients with posterior circulation obstruction were excluded because they were assessed using the pc-ASPECTS, which uses a different scoring method than DWI-ASPECTS. The IV rtPA was administered in 27 (47%) of patients.

The main occlusion site of large cerebral vessel was M1 part of middle cerebral artery in 35 (60.3%) patients. Only four (6.9%) of patients had occlusions in the posterior circulation. The most commonly used device for retrieval of thrombus was a stent retriever combined with an aspiration catheter. PTA was required in five (8.6%) cases with stenotic lesions due to atherosclerosis. A mean of 1.8 ± 1.1 retrieval procedures was required, and 53 (91%) of cases underwent successful reopening of TICI 2b or 3. The mean time from the onset to the recanalization was 323 ± 206 min, and from the puncture to the recanalization was 68.5 ± 33.4 min.

There were 19 (32.8%) cases of ICH associated with the MT as assessed using the T2*GRE. According to the Heidelberg classification of bleeding, Class 1a; scattered small petechiae in infarcted brain tissue, was found in two (3.4%). Class 1b; confluent petechiae changes in ischemic brain tissue, was found in nine (15.5%). Class 1c; hematoma within infarcted tissue which occupying the infarcted lesions, was founded in three (5.2%). Class 2; intracerebral hemorrhage within and beyond infarct-

ed brain tissue, was found in one (1.7%). Class 3 defined as subarachnoid hemorrhage (SAH) was found in four (6.9%). A class 2 patient was diagnosed with the only symptomatic ICH in this study because of increased NIHSS score due to impaired consciousness and worsening hemiparalysis after MT. Symptomatic ICH in this study was one patient (1.7%) and asymptomatic ICH, including SAH were 18 patients (31.0%).

Imaging Analysis

The chart presented the imaging flow of the DECT and T2*GRE analysis of 58 cases. High density area was detected on SECT in 22 of the 58 patients. Of these, 11 were DECT-positive and 11 were DECT-negative. Among the 11 DECT-positive cases, ten were diagnosed with hemorrhage and one without it. In the group diagnosed with hemorrhage, two cases were class 1b, three were class 1c, one was class 2, and four were class 3c according to the Heidelberg classification of bleeding. On the other hand, among the 11 DECT-negative cases, four were diagnosed with hemorrhage and seven was without it. In the group diagnosed with hemorrhage, all four cases were class 1b. Whereas there were 36 cases that did not show high density area on SECT, and there were no DECT-positive cases in these groups. But five of the DECT-negative 36 cases were eventually diagnosed as hemorrhage. In this hemorrhage group, two cases were class 1a and three cases were class 1b (Fig. 2). Illustration

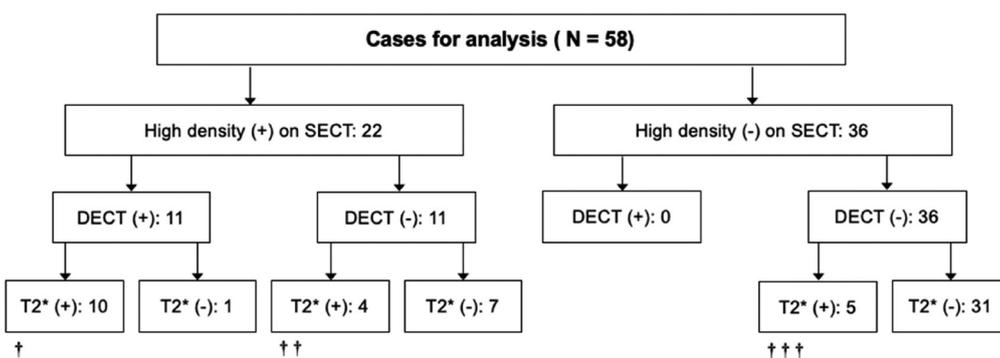


Figure 2. Flowchart of Analysis of DECT and T2*GRE

Patients had single-energy CT (SECT) and dual-energy CT (DECT) immediately after mechanical thrombectomy. T2*-weighted gradient-echo imaging (T2*GRE) were conducted within 24 h after the treatment for final evaluation of the intracranial hemorrhage. The type of hemorrhage observed in the SECT and DECT determinations is indicated in the figure based on the Heidelberg classification (HB class).

† : HB class 1b = two cases, HB class 1c = three cases, HB class 2 = one case, HB class 3c = four cases

† † : HB class 1b = four cases

† † † : HB class 1a = two cases, HB class 1b = three cases

tive DECT-positive and DECT-negative cases were demonstrated in Figure 3.

T2*GRE results corresponding to positive/negative DECT are shown in Table 2. According from the results, the diagnostic accuracy of DECT with

T2*GRE was a sensitivity of 52.6% (10/19), specificity of 97.4% (38/39), positive predictive value of 90.9% (10/11), negative predictive value of 80.9% (38/47) and accuracy rate of 82.8% (48/58) (Table 3).

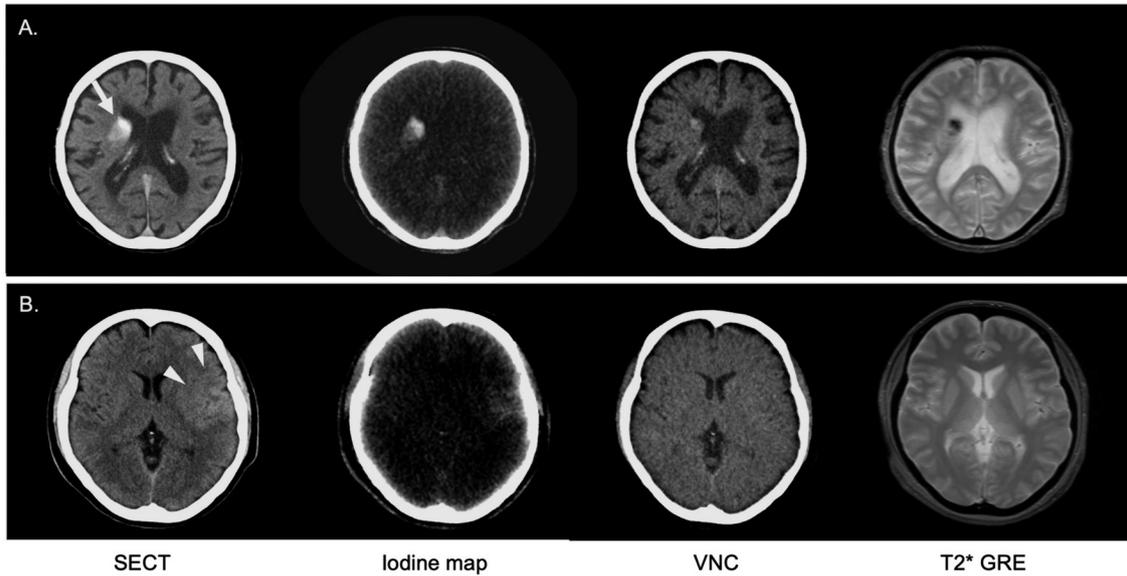


Figure 3. Illustrative Cases

A: patient with intracranial hemorrhage.

Single-energy CT (SECT) demonstrated high density area in right caudate head and basal ganglia (white arrow). Virtual non-contrast (VNC) constructed from dual-energy CT (DECT) also depicted high density lesion in same area that means DECT positive case. T2*-weighted gradient-echo sequence (T2*GRE) revealed intra-parenchymal hemorrhage depicted as low intensity area in the same location with VNC.

B: patient with extravascular leakage of contrast medium

SECT and iodine map demonstrated high density lesions in left insular, anterior and lateral part of middle cerebral artery perfusion area, and sylvian fissure (white arrow head). Although VNC did not detect high density lesion in same area that means DECT negative case. T2*GRE did not detect hemorrhage in this region.

Table 2. Cross tabulation table for DECT positive/negative group and Hemorrhage on T2*GRE

DECT \ Hemorrhage on T2*GRE	+	-	total
+	10	1	11
-	9	38	47
total	19	39	58

Abbreviations: DECT, dual-energy CT; T2*GRE, T2*-weighted gradient echo sequence

Table 3. Predictive value of MRI based evaluation of DECT for post mechanical thrombectomy hemorrhage

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
0.526	0.974	0.909	0.809	0.828

DISCUSSION

ICH is the most common complication associated with MT. The incidence is reported to be 5.7% for symptomatic ICH and 8.3% for SAH [4]. Another study reported a 41% incidence of asymptomatic ICH [18]. In our study, symptomatic ICH was present in 1.7%, SAH in 6.9%, and asymptomatic ICH, including SAH in 31.0%, which were comparable to previous reports.

Recurrent postoperative vessel occlusion is also another serious complication associated with MT. There are reported that the rate of recurrent occlusions after MT was 1.8%, the average time to recurrence was 2 days, and anticoagulants were not initiated in 74% of recurrent cases [19]. The recurrent large cerebral vessel occlusion inevitably worsens the neurological prognosis. To avoid this, it is desirable to start anticoagulant therapy as soon as possible after MT. However, early administration of anticoagulants to patients with hemorrhagic complications might have risks worsening ICH to be fatal. Therefore, it is very important to make an accurate differential diagnosis between postoperative hemorrhage and leakage of contrast agent. If diagnostic imaging can determine early initiation of anticoagulant, it should be very useful for perioperative management after MT. Although MRI has high diagnostic accuracy for ICH, and can be considered to be ideal choice for diagnosing hemorrhage after MT, it takes a long imaging time and it is difficult to observe the patient's condition in detail during the examination [20]. Furthermore, because patients with acute ischemic stroke immediately after the surgery are often unable to keep rest, it is hesitant to use MRI as a routine postoperative examination.

On the other hand, DECT has advantages as a post-MT imaging method because it can be performed in a short time and is less burdensome to patients and medical personnel. Recently, Chen *et al.* reported a systematic review of hemorrhagic events and contrast media leakage after MT with DECT [21]. Their review article demonstrated a sensitivity of 77% and specificity of 100% for DECT for hemorrhagic events and contrast media leakage after the MT. Moreover, the accuracy rate is as high as 89%–95%, indicating that DECT has ex-

cellent diagnostic ability [8, 22, 23]. But most of their reference images for VNC that were used to diagnose ICH were follow-up SECT images. Generally, extravascular leakage of contrast medium after neuroendovascular treatment is assumed to be differentiable via SECT reference images because the absorbed concentration of the contrast agent decreases with time. However, it must be considered that SECT may be difficult to detect small hemorrhages that may be absorb and disappear in a short period.

In our study, the sensitivity was 52.6%, specificity 97.4%, positive predictive value 90.9%, negative predictive value 80.9%, and accuracy rate 82.8%, which are not inferior to previous reports except sensitivity. Especially the specificity was high, suggesting that DECT is effective in excluding hemorrhagic complications immediately after MT.

We considered following two reasons for the lower sensitivity in our study compared to previous. First, it is the higher diagnostic accuracy of MRI for bleedings compared to SECT [24]. T2*GRE can depict micro hemorrhagic changes immediately after MT that cannot be detected by SECT. We believe that this study may have supplemented hemorrhagic lesions that could not have been detected in previous studies that used follow-up CT as a reference image for hemorrhage, and this may have contributed to the lower sensitivity in this study. Second, interval of DECT and MRI may affect results. In our study, 36 cases did not show high density lesions on SECT nor DECT. T2*GRE imaging found out that five of these 36 cases (13.8%) had ICH. The details of hemorrhagic cases corresponding the Heidelberg classification of bleeding were class 1a in two cases and class 1b in three cases. These classes may represent hemorrhagic changes caused by blood reperfusion blood into the ischemic brain with a damaged blood-brain barrier. And even if there is no immediate postoperative hemorrhage, these classes of hemorrhage could occur late. If DECT and MRI are performed simultaneously post-MT, some of these would not observe. The interval between the postoperative and the reference image may affect the diagnostic accuracy of DECT that was performed immediately after MT, so ideally both examinations should be done at the same time. However, it is necessary to establish a protocol that

allows patients to undergo MRI safely and stress-free immediately after surgery.

Present study demonstrates the high specificity of DECT for ICH after MT for acute stroke, but also suggests that it is still inferior to the diagnostic accuracy of MRI in the current era. We believe that DECT can be an alternative or complementary imaging method to MRI in the future if its characteristics are understood well. Also, the diagnostic accuracy of DECT may depend on the scanning method and type of CT equipment, and further study is necessary.

Study limitations

There were two limitations associated with the present study. First, the sample size was not large enough due to the short duration of the study and the number of enrolled cases. Analysis with larger sample volume might affect the diagnostic accuracy of DECT. Second, reading of DECT image was dependent on a radiologist. Since this is the study to evaluate the imaging accuracy, dependent and double imaging reading by two radiologists is preferred. Also, being a retrospective study is another limitation in our study.

CONCLUSION

This study revealed the high specificity of DECT for the diagnosis of hemorrhagic complications after MT for acute stroke based on MRI evaluation. And it was also demonstrated that the selection of reference images and the interval between DECT and reference images affect the diagnostic accuracy of DECT. Further study is necessary to understand the diagnostic accuracy and appropriate perioperative management after MT with DECT.

Ethical Approval

This study was approved by ethics committee of National Hospital Organization Hamada Medical Center (No. 0415), and Shimane University Faculty of Medicine (No. 20221019-2). All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. This study was a retrospective study, informed consent was obtained in the form of opt-out on the website.

Author Contribution

Hirotake EDA: Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing, Visualization.

Yoriyoshi KIMURA: Investigation, Writing - review & editing.

Kazuhiro YAMAMOTO: Investigation.

Kotaro YOSHIDA: Investigation.

Mizuki KAMBARA: Investigation.

Yasuhiko AKIYAMA: Writing - review & editing, Visualization, Supervision, Project administration.

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Conflicts of Interest

All authors have no conflicts of interest to declare.

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